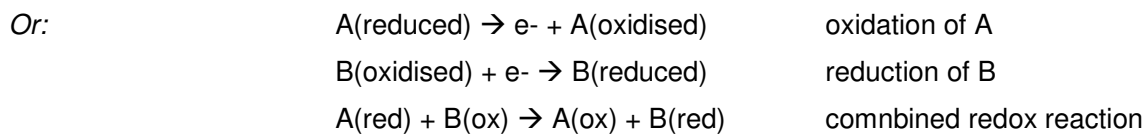
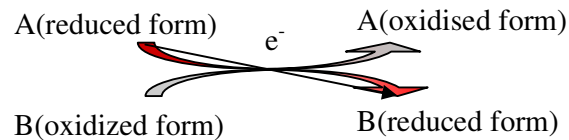


Ch 9: Cellular Pathways that Harvest Chemical Energy

1. Show, using a diagram, what happens in a redox reaction. Explain briefly.



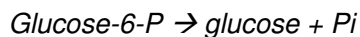
Electrons from A (in its reduced form) are transferred to the oxidised form of B. This results in oxidation of A and reduction of B. A compound is reduced when it accepts electrons and oxidized when it loses electrons.

2. Redox-reactions between metabolites in living cells are often coupled using mobile electron carriers. Name the two most important mobile electron carriers (A and B) in energy metabolism. A is water soluble and is found in the cytoplasm, while B is lipid-soluble and is found in the cell membrane in bacteria, and the mitochondrial inner membrane of eukaryotes.

A: NAD^+

B: *quinones (e.g. the nutritional supplement Q10 is a quinone that carries out electron transfer in the respiratory chain)*

3. Suggest reactions that do not involve oxidation or reduction, but where energy is released.



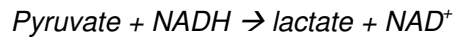
If an energy-rich bond is broken, energy is released. Acid anhydrides like phosphate-anhydrides (P-P bonds in ATP) are very energy-rich. Esters, particularly phosphate esters (O-P bond in glucose-6-phosphate) can also be very energy-rich.

4. What is the term “substrate-level phosphorylation” used to describe, and where/when is this process particularly important?

The term “substrate-level phosphorylation” describes all the processes where ATP is formed by phosphorylation of ADP, without involvement of a proton gradient, most importantly during glycolysis. The process is particularly important when respiration is not active, e.g. in muscle cells during hard work, where oxygen becomes limiting. In this case, energy is gained through substrate-level phosphorylation. See e.g. reactions in Fig 9.5 page 173.

5. How does a muscle cell benefit from producing lactic acid, and when does this occur?

If a muscle cell cannot respire due to lack of oxygen it will accumulate NADH and lack NAD^+ for glycolysis. By converting pyruvate to lactic acid (lactate), NAD^+ can be regenerated.

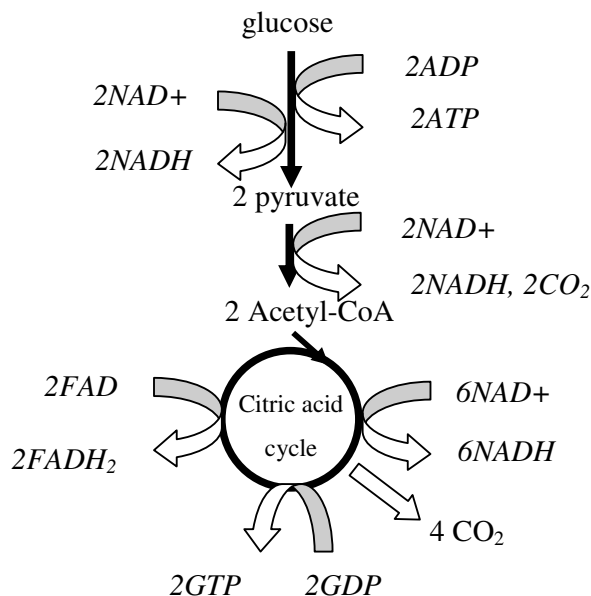


This is energetically inefficient because lactate, which is an energy-rich compound, is not further metabolised in the cell.

6. Explain which of the following statements about the citric acid cycle are correct:

- occurs in mitochondria yes
- does not produce ATP not directly, but GTP is produced
- has no connection with the respiratory chain yes, it produces NADH which feeds the respiratory chain
- is the same as fermentation no

7. In a simplified representation, glycolysis is often represented by an arrow, the citric acid cycle by a circle and the most important substrates and products are given. Add the most important substrates and products to this drawing:



8. Several enzymes in glycolysis and the citric acid cycle are allosterically regulated.

- How does allosteric regulation function?

A regulatory molecule binds to a specific regulatory site on the enzyme (not the active site). This causes a conformational change, that either activates or inhibits the normal function of the enzyme.

- Why is it advantageous for the cell, that enzymes in these pathways are activated by AMP and ADP or are inhibited by ATP?

This means that glycolysis is most active when there is a low ATP:ADP ratio – ie insufficient energy for ATP synthesis. When the ATP:ADP ratio is high the cell has sufficient energy and glycolytic activity is reduced.

- Why is it advantageous for the cell, that enzymes in the citric acid cycle are activated by NAD^+ or are inhibited by NADH?

A low NADH/NAD^+ ratio suggests that glycolysis and the citric acid cycle are unable to produce enough NADH to supply the respiratory chain – as soon as it is produced, it is oxidised to NAD^+ . Therefore it would be an advantage for the cell to increase the activity of the citric acid cycle. On the other hand, a high

NADH/NAD⁺ ratio suggests that the respiratory chain cannot oxidize all the NADPH produced, in which case it would be advantageous to lower the activity of the citric acid cycle.

9. Which of the following possibilities give the greatest energy yield to an animal cell, if it has sufficient NAD⁺ and ADP, but neither NADH or ATP (explain your answer):

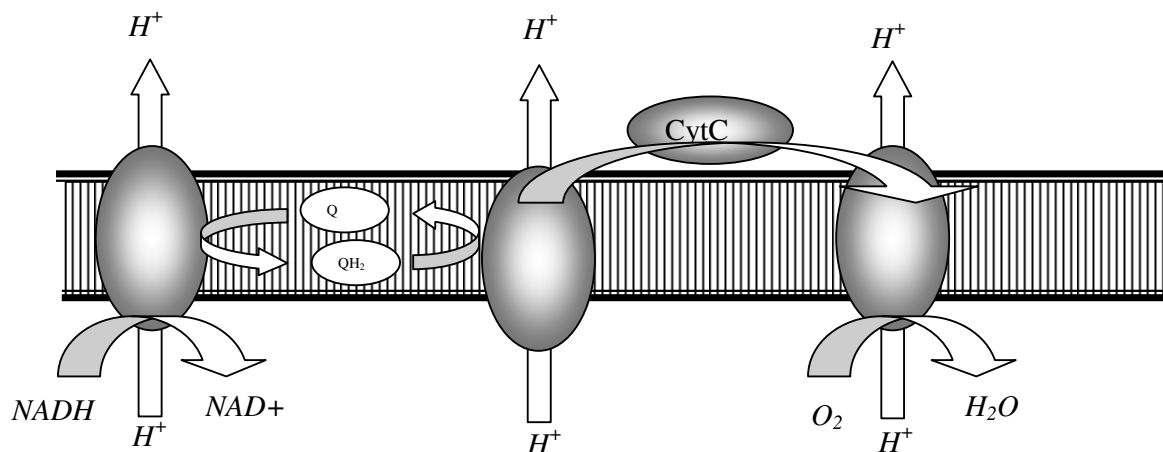
1) The addition of x mol ATP

2) The addition of x mol NADH

2)

Animal cells can respire, and therefore oxidise NADH while generating a proton gradient. This proton gradient can then be used to synthesise ATP from ADP. For each NADH that is oxidized by the electron transport chain, 2.5 molecules of ATP are formed. Most energy can therefore be obtained from x mol NADH which can be used to form 2.5x mol ATP. See the energy budget in fig 9.13

10. Label the missing molecules on the following diagram of the respiratory chain:



11. How do cells attain redox balance (ratio between oxidation and reduction) during respiration and fermentation, respectively?

During respiration: by oxidation of NADH in the respiratory chain using O₂ as oxidizing agent

During fermentation: by reduction of pyruvate to lactate (or ethanol) with oxidation of NADH

12. Explain the difference in ATP production per glucose by:

a) substrate-level phosphorylation

b) respiration.

a) 2 molecules ATP and 2 molecules lactate (which is discarded) are produced per glucose by substrate-level phosphorylation in glycolysis and fermentation

b) When pyruvate is broken down through the citric acid cycle, in addition to the 2 molecules ATP generated by glycolysis, in total 10 NADH + 2 FADH₂ + 2 GTP are produced. By respiration of the NADH and FADH₂ a proton gradient is formed that is used to generate about 28 ATP, in total 32 ATP.

13. Commitment step

a) What is "the commitment step"?

The commitment step is the first enzyme-catalysed step in the metabolic pathway which is specific for that pathway and beyond which there is "no way back". All following reactions run until the product is obtained.

b) Why is the commitment step usually the step in a pathway that is subject to regulation?

By regulating the commitment step, the whole pathway is controlled and it is not necessary to regulate the following reactions.

c) Which reaction is the commitment step for glycolysis?

Conversion of fructose-6-phosphate to fructose (1,6)-bisphosphate (Fig 9.5 p 173, reaction no. 3). The commitment step is the first step specific for a single pathway, such that there is only one possible product formed (in this case pyruvate). Glucose-6-phosphate is used in other pathways in addition to glycolysis and is therefore not the commitment step in glycolysis. The PFK-catalysed reaction determines how much glucose is funneled through glycolysis (p. 186) and is the commitment step.

d) Which enzyme catalyses this reaction, and how is it regulated?

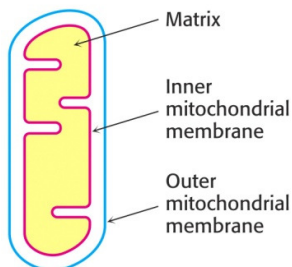
The reaction is catalysed by phosphofructokinase. this enzyme is allosterically inhibited by ATP and activated both by ADP and AMP. The enzyme is also feedback-regulated by citrate. Fig 9.16 p 186

Example exam questions

1. Which of the following statements about the respiratory chain are correct?

- occurs in mitochondria **Yes - (in eukaryotes)**
- uses O₂ as oxidising agent **Yes**
- regenerates oxidising agents for glycolysis and the citric acid cycle **Yes**
- occurs at the same time as fermentation **No**

2. Sketch the position of ATP synthase in the mitochondrial membrane and briefly describe the function of the enzyme.



See fig 9.9 p 179.

3. Where in a eukaryotic cell do the following occur?

- a) citric acid cycle? **In the mitochondrial matrix**
- b) glycolysis? **Cytoplasm**
- c) elektron transport chain? **In the mitochondrial inner membrane**

4. The following reactions may occur, after a polysaccharide has been broken down to monosaccharides like glucose:

Reaction 1: phosphoenolpyruvate → pyruvate

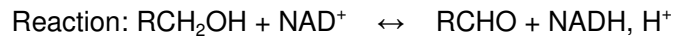
Reaction 2: pyruvate → lactate

Explain briefly the significance of each of these reactions for the energy metabolism of the cell.

Reaction 1: **This reaction results in the formation of ATP and occurs both under aerobic and anaerobic conditions.**

Reaction 2: **This reaction enables regeneration of NAD^+ from NADH. NAD^+ can then be used for glycolysis. This reaction occurs under anaerobic conditions and is called fermentation. The reaction itself does not yield energy, but is necessary for maintenance of glycolysis and to prevent accumulation of NADH. Fig 9.11 p 182.**

5.



- a. State which is the reduced and oxidized form of each molecule in this reaction.

NAD^+ is the oxidised form, NADH is the reduced form.

RCH_2OH is the reduced form – RCHO is the oxidised form

- b. What does the abbreviation "NAD⁺" stand for?

Nicotinamide Adenine Dinucleotide

6. Glucose can be converted by our metabolism to CO_2 and H_2O . Is the overall reaction an oxidation or reduction? Explain your answer.

Overall, this is a redox reaction where glucose is oxidised to CO_2 , and O_2 is reduced to water.